REMARKS

Claims 1-115 are pending in this application; Claims 4-6, 10-12, and 15-115 having been withdrawn by the amendment of 12 June, 2006.

Applicants acknowledge the Examiner's consideration of the IDS forms dated 30 October 2006.

The Examiner requested the date of the publication cited in the IDS Reference A159. The date of publication of reference A159 is March 1, 2004, which is the date of the submission of the grant. The Examiner is respectfully requested to enter the reference A159 into the IDS of record.

Applicants thank the Examiner for noting the typographical error in Claim 6, and the correction will be made as needed in a future response, as Claim 6 has been withdrawn from Examination in the present application.

Rejection under 35 U.S.C. 103(a)

In the present Office Action, the Examiner rejected Claims 1-3 and 13 under 35 U.S.C. 103(a) as being unpatentable over Thorpe et al. (US 5,762,918, referred to hereinafter as "US '918"), Janda et al. (US 6,664,372, referred to hereinafter as "US '372"), and Pouyani et al. (US 5,616,568, referred to hereinafter as "US '568").

Claims 7-9 and 14 are objected to for dependency on rejected claims.

On pages 3-4 of the Office Action, the Examiner alleges that US '918 discloses a "thiol-reactive electrophilic functional group" which renders the claimed compositions obvious because the claimed electrophilic moiety is not required to be carbon. In view of the present amendments to Claim 1, Applicants respectfully traverse the rejection of Claim 1-3 and 13 under 35 U.S.C. 103(a).

In the present Office Action, the Examiner rejected Claims 1-3 and 13 under 35 U.S.C. 103(a) as being unpatentable over US '918. The Examiner has not cited US '928 in combination with any other art references.

Applicants respectfully submit that US '918 not only does not anticipate the composition of the present invention, US '918 does not suggest or motivate one skilled in the art to prepare the composition as recited in the present invention. On page 3 of the Office Action, the Examiner alleges that while Q can be a sulfhydryl group, Q can also be a "thiol-reactive electrophilic functional group" as recited in Claim 1. Accordingly, the Examiner suggests an equilibrium disulfide reaction (see below) between a disulfide and a free thiol compound and conclude that because one of the sulfur atoms of the disulfide moiety qualifies as a "thiol-reactive electrophilic functional group," it follows that US '918 renders Claims 1-3 and 13 obvious.

$$R^4\text{-S-S-}R^5 \quad + \quad R^6\text{-SH} \quad \rightarrow \quad R^4\text{-S-S-}R^6$$

$$R^4\text{-S-S-}R^6 \quad + \quad R^5\text{-SH} \quad \rightarrow \quad R^4\text{-S-S-}R^5$$

However, as amended, Claim 1 presently do not recited that the Q group may be a "thiol-reactive electrophilic functional group" as defined on page 6, paragraph [0100] in the present specification (US 2005/0176620). Claim 1, as presently amended, define the Q group as follows:

> "Q is a SH group, or is selected from the group consisting of $C_{1\text{-}24}$ alkyl halide, $C_{1\text{-}24}$ alkoxy-$C_{1\text{-}24}$ alkyl, α-halocarbonyl, maleimides, vinyl sulfones, acrylonitriles, α-methylene esters, quinine methides, acryloyl esters, acryloyl amide, α-halo esters and α-halo amides, and …"

As exemplified above, Q has been amended to limit the scope of the possible functional groups as explicitly recited, and Q is no longer generally defined as a "thiol-reactive electrophilic group." Clear and explicit support for the amendment in Claim 1 may be found in the definition of the term "thiol-reactive electrophilic group" on page 6, paragraph [0100] of the present application published as US 2005/0176620.

Accordingly, as amended, Claim 1 no longer recites the limitation that Q is a "thiol-reactive electrophilic group" that may possibly be defined as a disulfide group as the Examiner alleges; and none of the recited groups defined by Q include a disulfide group as cited in US '918. Because Claim 1 no longer defines the group Q as a "thiol-reactive electrophilic group", Q can not be construed to be a disulfide group as disclosed in US '918.

Furthermore, US '918 is directed to the compositions of derivatives of heparin conjugated to anti-angiogenic steroids for the purpose of delivering the anti-angiogenic steroids to vascular endothelial cells. See claim 1 and Examples I-VI, column 22-37 of US '918. Accordingly, US '918 does not suggest the compound of the present application that is recited in Claim 1, wherein the compound is a residue of a macromolecule linked to a -C(=O)-NH-NH-(C=O)-L-Q, where Q is as specifically defined above and do not include an anti-angiogenic steroid or any steroid for that matter.

With respect to the specific examples cited by the Examiner on page 3 of the Office Action, Applicants respectfully note that these compositions, requiring both a heparin substituent as well as a disulfide linkage to a pyridine, phenyl or ricin substituent, are structurally distinct to the conjugate of the present invention, shown in Formula I of Claim 1. The compound of Claim 1 in the present application do not include both a heparin with a disulfide linked to a pyridine, phenyl or ricin substituent.

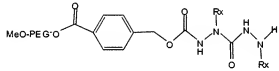
The Examiner has not shown that there is some suggestion or motivation within US '918 or in the knowledge of the art to combine the US '918 with any other art references to render the present claims obvious. In addition, the Examiner has not shown that there would be a reasonable expectation of success if US '918 and any other references were to be combined, and the Examiner has also not shown that the combination of US '918 and any other art would teach or suggest all the limitations of Claim 1 or its dependent claims. Accordingly, US '918 does not teach or disclose all aspects of the present invention as recited in Claim 1. And because Claims 2, 3 and 13 are dependent on Claim 1, Applicants respectfully assert that Claims 2, 3 and 13 are also not obvious in view of US '918.

The Examiner is respectfully requested to reconsider and withdraw the rejection of Claims 1-3 and 13 under 35 U.S.C. 103(a).

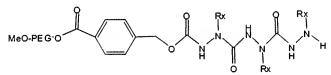
On page 4 of the Office Action, the Examiner rejected Claim 1 under 35 U.S.C. 103(a) as being unpatentable over US '372. according to the Examiner, US '372

> "discloses a compound which contains the requisite dicarbonyl hydrazine group. At one terminus of the compound there is a variable "Rx"; it is recited at col 4, line 62 that this Rx group can be the side chain of cysteine."

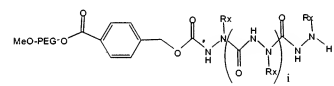
Applicants note that the compounds disclosed in US '372, as referred to by the Examiner, are "oligoazatide compounds" (see column 4, line 49) because, where i is 0, I is 1 or where I is ≤99, then the compound has the structure of either A, B or C below:



A



B



C

As apparent from the structures of the compounds shown above, where i is 0, 1 or ≤ 99, the compounds disclosed in US '372 are dihydrazides, tri-hydrazides or poly-hydrazides. On the other hand, the compound recited in Claim 1, as presently amended, has the corresponding group "–L-Q" wherein the group –L-Q corresponds to the explicitly listed functional groups, none of which are dihydrazides, tri-hydrazides or poly-hydrazides.

In view of the amendment to Claim 1 and the clear distinctions between the compounds of the present Claim 1 and the disclosure of US '273 as noted above, Applicants respectfully assert that the present claims are not obvious in view of US '392. And because

Claims 2, 3 and 13 are dependent on Claim 1, Applicants respectfully assert that Claims 2, 3 and 13 are also not obvious in view of US '392. Examiner is respectfully requested to reconsider and withdraw the rejection of Claims 1-3 and 13 under 35 U.S.C. 103(a).

On page 4 of the Office Action, the Examiner rejected Claims 1-3 and 13 under 35 U.S.C. 103 as being unpatentable over US '568.

According to the Examiner, US '568 teaches in structure 2e, column 12, a compound that falls within the scope of Claim 1 because "a disulfide bond qualifies as a "thiol-reactive electrophilic functional group." However, as noted above with respect to the presently amended Claim 1, Q has been amended to limit the scope of the possible functional groups as explicitly recited, and Q is no longer defined as a "thiol-reactive electrophilic group." Accordingly, as amended, Claim 1 no longer recites the limitation that Q is a "thiol-reactive electrophilic group" that may possibly be defined or construed as a disulfide group as the Examiner alleges; and none of the explicitly recited groups of the variable Q in Claim 1 include a disulfide group as cited in US '568.

In addition, compound 2e of US '568 contains two hyaluronic acid group (i.e. "HA") at each of the terminal ends of compound 2e, while the compound of Claim 1 in the present application clearly do not have the two HA groups. In addition, compound 2e has a specific structure that is clearly symmetrical about the disulfide group, while the compound as recited in Claim 1 does not have a structure that is symmetrical about a disulfide bond and is clearly distinct from the structure of compound 2e. Applicants respectfully assert that such compounds as taught in US '568 alone or in combination of any other (un-cited) art reference do not render the compound of Claim 1 obvious.

The Examiner further noted that "there is a hydrocortisone/hemisuccinate/hyaluronate conjugate provided in the space spanning cols 21-22 (approx line 15+)" in US '568. And "as it happens, there are three separate sites that would qualify as a "thiol-reactive electrophilic functional group."" In particular, the Examiner cites the ester bond, the position which is alpha to the exocyclic keto group of the hydrocortisone, and the enone present in the hydrocortisone of US '568.

However, as noted above, as presently amended, Claim 1 no longer recites a limitation in which the group Q is a "thiol reactive electrophilic functional group" and accordingly, the group Q now does not recite the functional limitation that Q is a thiol reactive electrophilic functional group. Rather, Q now recites a specific and limited number of selected functional groups, none of which are the same or even similar to the groups cited by the examiner.

Accordingly, Applicants respectfully assert that such compounds as taught in US '568 alone or in combination of any other (un-cited) art reference do not render the compound of Claim 1 obvious. And because Claims 2, 3 and 13 are dependent on Claim 1, Applicants respectfully assert that Claims 2, 3 and 13 are also not obvious in view of US '568.

The Examiner is respectfully requested to reconsider and withdraw the rejection of Claims 1-3 and 13 under 35 U.S.C. 103(a) in view of US '568.

Applicants respectfully assert that nothing in the cited art references US '918, US '372 and US '568 alone or in combination with any cited art, suggest the desirability of forming the compounds of the application, except, of course, the disclosure of the present application, which may not be used as a basis to guide the combination.

In view of the foregoing amendments and remarks, Applicant submits that all of the claims are in proper format and are patentably distinct from the prior art of record and are in condition for allowance. Applicants respectfully request withdrawal of the rejection of Claims 1-3 and 13 under 35 U.S.C. 103(a) and the objection to dependent Claims 7-9 and 14.

CONCLUSION

Entry of the amendments, and reconsideration of the rejection of Claims 1-3 and 13 and corresponding objection to dependent Claims 7-9 and 14 in view of the foregoing amendment and remarks, and allowance of the claims are respectfully requested. In view of the foregoing remarks, reconsideration of the application and allowance of elected claims is requested.

If there are any issues remaining that the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the contact information listed below.

Date: March 27, 2007

Respectfully submitted,
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